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Award Number: W81XWH-08-2-0133

TITLE: MISSION CONNECT MILD TBI TRANSLATIONAL RESEARCH CONSORTIUM

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REPORT DATE: August 2009

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
08-31-2009	Annual	08-01-2008 - 07-31-2009

4. TITLE AND SUBTITLE

MISSION CONNECT MILD TBI TRANSLATIONAL RESEARCH CONSORTIUM

5a. CONTRACT NUMBER
W81XWH-08-2-0133

5b. GRANT NUMBER
PT074693P2

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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820 Chandler Street
Fort Detrick, MD 21702-5014

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Distribution is unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This report outlines Dr. Levin's participation in the Mission Connect Mild Traumatic Brain Injury (TBI) Translational Research Consortium during the time period of August 1, 2008 through July 31, 2009. The first year of work on this project has involved substantial collaborative effort to compile research activities from the clinical investigators into a single, unified protocol and to obtain the required institutional approvals. Research activities from Specific Aims 2.1 (Levin), 2.2 (Masel), 2.3 (Papanicalaou), and 3.1 (Robertson) were compiled and organized into the Integrated Clinical Protocol in order to 1) minimize the burden of participation for subjects, 2) streamline and coordinate procedures whenever possible, and 3) use resources effectively, particularly study personnel. In addition, the majority of work to define and prepare for subject recruitment, scheduling, and follow-up has been accomplished, and the implementation of a comprehensive data management plan that supports this project and all the clinical investigators is being implemented.

15. SUBJECT TERMS
None provided.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		5	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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INTRODUCTION: This report outlines Dr. Levin's participation in the Mission Connect Mild Traumatic Brain Injury (TBI) Translational Research Consortium during the time period of August 1, 2008 through July 31, 2009. The long-term goal of the Consortium is to improve the diagnosis and treatment of MTBI through collaborative basic and clinical research by experienced TBI investigators. Dr. Levin is the PI for Specific Aim 2.1, which focuses on analysis of early (< 24 hours) MTBI and differentiation of brain injury sequelae from post-traumatic stress disorder (PTSD) symptoms. The research activities for Specific Aim 2.1 are being conducted in collaboration with the other clinical projects in the Consortium: Specific Aims 2.2 (PI Papanicalaou), 2.3 (PI Masel), and 3.1 (PI Robertson) as the Integrated Clinical Protocol. The Integrated Clinical Protocol consists of three observational studies (Specific Aims 2.1, 2.2, and 2.3) and one Phase II randomized clinical trial (Specific Aim 3.1) that will use a shared group of subjects. Two hundred subjects with mild TBI and 100 subjects with orthopedic injury (OI) without TBI will be recruited (NOTE: The OI subjects will not participate in the medication trial). Dr. Levin also directs the Neuropsychology Core, which is responsible for subject recruitment and follow-up for all the clinical projects in the Integrated Clinical Protocol, as well as conducting all neuropsychological testing.

BODY: The first year of work on this project has involved substantial collaborative effort to compile research activities from all the clinical investigators into a unified protocol and to obtain the required institutional approvals. As of July 29, the Integrated Clinical Protocol has received approvals from two local institutional review boards (May 4, 2009) and from HRPO (July 15, 2009). Preparatory activities for subject recruitment and data management have been conducted concurrently with this approval process, including the logistics of subject recruitment and management, development of required case report forms and other study documents, and design of electronic data collection/management systems. Pending local IRB approval of the modifications required by HRPO, we are ready to begin subject enrollment.

Specific Aim 2.1: Dr. Levin's work in this reporting period has been directed toward three specific objectives:

1. Differentiation of MTBI from non-brain injury trauma on cognitive performance, DTI, and EEG
2. Differentiation of PCS and ASD after brain injury and orthopedic injury
3. Identification changes in cognitive performance, PCS, PTSD symptoms, depressive symptoms, and functional outcome

Detailed study procedures and logistical plans have been developed to accomplish these objectives, in conjunction with the other Aims in the Integrated Clinical Protocol. To date, we have:

- Developed of a single, unified Protocol. Research activities from the four clinical specific aims were compiled and organized into the Integrated Clinical Protocol. Our goals were 1) to minimize the burden of participation for subjects, 2) to streamline and coordinate procedures whenever possible, and 3) to use resources effectively, particularly study personnel. This was a highly challenging task, as each investigator had prepared their Statement of Work independently for the application. In the process of developing this Integrated Clinical Protocol, opportunities for sharing of data and personnel have resulted in a number of significant operational efficiencies. The Clinical Working Group has been the primary venue where this work was accomplished.
- Established of Study Procedures. From the finalized Integrated Clinical Protocol, comprehensive standard operating procedures (SOPs) for study activities have been developed for 1) start-up procedures, 2) subject screening and enrollment, and 3) each of the five study visits (Baseline, 1 Week follow-up, 1 Month follow-up, 3 Months follow-up, and 6 Months follow-up).
- Designed a Data Management Plan. A comprehensive data management plan has been developed to create a comprehensive data set, based on the needs of investigators to access the data of their colleagues, as well as their own. In addition, this plan is designed with all necessary procedures to ensure subject privacy and data confidentiality, compliant with HIPAA, FDA and ICH GCP regulations

and guidelines. Silverwind Research, Inc., of La Veta, Co, has been selected to provide these services. We are finalizing data needs and requirements for all investigators participating in the Integrated Clinical Protocol. Data lists, variable definitions, and a data dictionary are being prepared. Requirements for Case Report Forms have been provided to Silverwind.

Neuropsychology Core: During this reporting period, activities have been directed toward:

- Staff recruitment, employment, organization, training. One full-time Research Nurse and two Research Coordinators III have been hired, and they are actively involved in the development of study documents and procedures. We are actively recruiting for an additional full-time Research Nurse. This opportunity has been posted with the Human Resources Department.
- Subject Recruitment, Enrollment, and Management. The following start-up procedures have been developed and are ready for subject enrollment, including:
    - Emergency Department (ED) liaison: Subjects for the Integrated Clinical Protocol will recruited in the Emergency Department.
    - Use of Clinical Research Unit: Subjects will be screened and enrolled in the ED, but their participation will not begin until after discharge. The Clinical Research Unit of the University of Texas will be used as the location for conducting the neuropsychological testing and other study procedures. Detailed procedures have been developed and approved.
- Establishment of Inter-rater Reliability. In collaboration with the project statistician, Dr. Paul Swank, a comprehensive plan to ensure data reliability is in progress. The plan addresses major sources of variability unrelated to the hypotheses, including inter-rater reliability, variability in test administration, and scoring variability, both at project initiation during ongoing data collection. The initial stages of the plan (training in task administration, training in scoring, and establishment of inter-rater reliability) have been implemented.

KEY RESEARCH ACCOMPLISHMENTS:

- Collaborated with other investigators to develop the Integrated Clinical Protocol
- Developed a comprehensive data management plan, selected a data management services vendor, and initiated work on the automated data collection/management system
- Participated in regular meetings of the Clinical Working Group
- Contributed to the design/development of case report forms and automated data entry procedures

REPORTABLE OUTCOMES:

- IRB approval of the Integrated Clinical Protocol was received on May 4, 2009, at both participating institutions, Baylor College of Medicine and the University of Texas Health Sciences Center at Houston
- HRPO approval of the Integrated Clinical Protocol was received on July 15, 2009. The required changes and modifications have been submitted to both local IRBs.

CONCLUSION: The first year of work on this project has involved substantial collaborative effort to compile research activities from all the clinical investigators into a unified protocol and to obtain the required institutional approvals. In addition, the majority of work to define and prepare for subject recruitment, scheduling, and follow-up has been accomplished, and the implementation of a comprehensive data management plan that supports this project and all the clinical investigators is being implemented.

REFERENCES: none

APPENDICES: none

SUPPORTING DATA: none